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ENVIRONMENTALLY SOUND MANAGEMENT OF BIOTECHNOLOGY

BACKGROUND AND ISSUES

Report of the Secretary-General of the Conference

INTRODUCTION

1. At its second substantive session, the Preparatory Committee requested the Secretary-General of the Conference to elaborate on the environmentally sound management of biotechnology for discussion at its third session, taking into account decision 1/17 and General Assembly resolution 44/228.
2. This report elaborates on the potential for environmentally sound applications of biotechnology as well as the methodologies and procedures that could be used internationally to assess and manage biotechnology risks; which were proposed in document A/CONF.151/PC/29 for the second session of the Preparatory Committee.
3. This report takes into account the work undertaken by the UNIDO/UNEP/WHO/FAO informal working group on safety in biotechnology, the Organisation for Economic Cooperation and Development, the results of regional meetings organized by the United Nations Economic and Social Commissions, other relevant organizations, as well as the advice of the Working Party on Biotechnology.

4. This report also reflects the advice and comments given by the participants of the Senior Level Expert Workshop on Assessing and Managing Biotechnology Risks. The ad hoc Workshop, organized with the support of the Government of the United Kingdom, was attended by over 40 participants from 30 countries, of which 13 were from developing countries.

PART I

ENVIRONMENTALLY SOUND APPLICATIONS OF BIOTECHNOLOGY

THE POTENTIAL OF BIOTECHNOLOGY

5. Developments in biotechnology offer unique solutions to increasing food security, for example, by biological pest control, efficient bio-fertilization, genetically modified insect and herbicide resistance in crops. New methods of detecting and incorporating useful genes of economic importance in both plants and animals make it possible to create and release new plant and animal varieties. New techniques that significantly shorten the time required to create improved varieties hold the promise of making available higher productivity varieties for cultivation under marginal conditions of moisture, temperature and nutrition that prevail in many developing countries. Improving the quality of agricultural and animal products through genetic modification is another important area of development.

6. Most nations, especially developing countries, have abundant water resources and certain types of land for much greater production of food and other commodities through aquaculture, agriculture, and horticulture. New technologies for the large-scale production of fast growing multi-purpose trees and biomass can revolutionize afforestation and green cover efforts, leading not only to environmental improvements but also to economic returns for the people who depending on these resources.

7. Newer technologies in animal breeding through embryo-based intervention have already demonstrated greater productivity. Use of growth hormones and their analogues are coming into agricultural practice. Development of monoclonal antibodies and DNA probe based diagnostics are increasingly used for detecting disease and superior varieties of plants and animals. Similarly newer and improved vaccines are protecting animals more effectively. New approaches to germ plasm collection, storage, and retrieval make available an enormous pool of genes of economic importance for breeding purposes.

8. Significant developments have already been witnessed in the area of human health in the form of new and improved vaccines that are safer and more protective against a host of communicable diseases. New developments in immunology have led to protection against several diseases through the use of single polyvalent vaccines. More and more vaccines are being delivered orally, thus preventing the risk of injections. The coming decade promises to make available protective vaccines against parasitic and protozoal diseases and against some viruses such as AIDS. Enormous progress has already been seen in the area of diagnostics using both monoclonal antibodies and nucleic

acid probes. Already the sales turnover in this area exceeds \$US 1.5 billion per annum. Products are already being tested or available, such as hormones, growth promoters, and factors controlling, promoting, or inhibiting cell proliferation. Attempts at developing safe, reversible and highly effective new contraceptive agents could strengthen family planning programmes. Products for treating infertility are also in an advanced state of development.

9. A large number of technologies based on new and improved microbial systems have already been developed for the safe treatment of industrial and urban effluents and pollutants. These technologies also generate useful by-products such as energy, fertilizers and clean recyclable water. The major approach to maintaining a cleaner environment is to deal with effluents, pollutants and residues as resources that can be treated to make safe, useful and recyclable end products.

10. The future holds significant promise for a variety of products for the early detection of pollutants and development of products, as well as health monitoring using bio-sensors, bio-chips, and bio-electronics. Technologies for enhanced oil recovery, microbial mineral and ore leaching that require much less energy are already available.

11. Biotechnology has wide application in several sectors of great economic relevance for both developing and developed countries. It is generally skill and not capital intensive. It generates employment and at the same time is also capable of miniaturization and automation. It can be applied either in the decentralized, rural environment or set up in a modern urban industrial complex. While the development of the technologies and products is still intensive, its products can be used by untrained people. The development and application of biotechnology is location specific and may lead to sustainable use of industrial resources.

12. Biotechnology, if used with care and appropriate management and monitoring practices, may provide acceptable risks to human health and the environment. The applications described in this report could lead to the proper utilization of the environment and the resources on this planet for the benefit of society, both present and future.

SOME APPLICATIONS

13. Health: The application of biotechnology to the area of human health has seen the most benefits. The applications are numerous and many of the benefits derived are quite spectacular. A summary of applications prepared as early as 1982 already showed results in many different areas.

- a. Monoclonal antibodies (for purification techniques, assays, tissue typing, in vivo tumor location, clinical diagnosis, therapy including targeting of chemotherapeutic agents);
- b. Interferon (possible use for cancer treatment, antiviral therapy, inflammatory diseases);
- c. Vaccines (e.g. against hepatitis B, influenza, encephalitis, cholera, herpes, adenovirus);

- d. Hormones (e.g. growth hormones, insulin, prolactin, relaxin, gastrin, erythropoietin, thrombopoietin, chorionic gonadotropin, menopausal gonadotropin, steroids);
- e. Enzymes (e.g. urokinase, heparinase, alcohol dehydrogenase);
- f. Other proteins (e.g. specific antigens, blood factor, albumin, antithrombin, fibronectin);
- g. Improved and new antibiotics, drugs, vitamins;
- h. Gene therapy for genetic diseases.

14. By 1982, the contribution of medical and pharmaceutical products accounted for approximately 2 per cent of total exports and imports of OECD Member countries. Sales of four new classes of antibodies was in excess of \$US 4 billion.

15. The potential for developing new or improved vaccines against common diseases of worldwide importance has been studied. Some aspects considered include the cost of research and development, the cost of the vaccine itself, time-frame for development, and delivery techniques.

16. Several other products of therapeutic importance have also been realized, for example, Tissue Plasminogen Activator, interferon, growth hormone, cell proliferation factors. Several more are in an advanced stage of development and are expected to reach the market in the next few years.

17. Another area in which biotechnology products have been successfully marketed is monoclonal antibodies for diagnostics and basic research. In the fast developing area of new drug design using computer modelling, site directed mutagenesis and receptor interaction, several new drugs that have greater specificity, safety and lower dosage requirements are at an advanced stage of development and are expected to revolutionize new drug development.

18. Food, Agriculture, and Horticulture: Modern techniques of biotechnology are being used in major applications in agriculture to create new strains of crop plants, new plant and animal diagnostic products, animal vaccines, biological pesticides and herbicides, other biological control agents, and modifications in domestic animals used for food production. Genetic modification in plants may be done at three levels; molecular, cellular, or organismal; each at least a few different applications of biotechnology.

19. Transgenic Plants: From a practical point of view, the availability of transgenic (genetically modified) crops that have already undergone successful field testing is the best indication of recombinant technologies that can be shared and introduced in developing countries in the near future. Some specific information on field-tested transgenic plants has already been evaluated in the developed countries. A total of 15 transgenic crops have already been field tested. The most intensive field tests have been conducted for potato and tobacco (in most instances the latter serving as a model crop for genetic modification) followed by oil seed rape, alfalfa, and corn. More

limited field testing has been conducted with cantaloupe, cucumber, poplar, soy bean, squash, and walnut. Most of the near future opportunities are in vegetables and fruits (potato, tomato, cucumber, cantaloupe, and squash), followed by legumes (alfalfa) and vegetable oil crops (oil seed rape).

20. Nine traits have been incorporated and field tested in a total of 15 crop plants. It is notable that two thirds of the traits are related to biotic pest stresses and that approximately one half of the crop/trait combinations are resistances to plant disease, mainly virus diseases and insect pests. There are also increasing numbers of transgenic plants with quality-related traits and resistance to abiotic stresses and male sterility.

21. Joint consideration of crops and specific traits allows near future opportunities for using recombinant technology to be assessed more carefully. Much Information has been collected from approximately 200 field tests from more than 10 countries over a six-year period. In OECD countries alone over 400 experimental introductions of agricultural plants with modified traits have occurred. Many of these crops are among those being currently introduced. 1992 will see the first introduction of crops in performance trials on a large scale.

22. The most important near future opportunities are for virus resistance and insect pest resistance in horticultural crops (vegetables and fruit), followed by cotton, oil seed rape and alfalfa. While herbicide resistance has been incorporated and field tested in many crops, it is a different and more complex application than virus and insect pest resistance with additional implications for sustainable development and environment protection. On the other hand, improved resistance to virus diseases and insect pests by genetic modification represent an opportunity for recombinant technology to make an important near future and positive contribution to sustainable development and environment protection by decreasing the dependency on insecticides, in both the industrialized and developing countries. Indeed improved resistance from viruses and insects through genetic modification may be one of very few technologies that can contribute to sustainable development in the short term.

23. Of the \$US 23 billion spent on pesticides annually approximately one quarter is sprayed on vegetables and fruit crops that are intensively managed. In developing countries, they are grown by the smaller, poorer farmers who are exposed to the many hazards associated with spraying pesticides. This includes hazards to the producers, consumers, and to the global environment, as pesticides are accumulated in the food chain, soil, and water resources. Similarly, approximately 10 per cent of global pesticides are applied to cotton to control a variety of insect pests. A significant proportion of the world's cotton is grown in developing countries which are not well-equipped to apply pesticides and can least afford the foreign exchange required to purchase imported pesticides. Therefore, it is important to utilize field tested transgenic vegetable, fruit, and cotton plants with incorporated selected virus and insect resistance to significantly decrease the dependency on insecticides for the control of specific virus vectors and insect pests.

24. Non-conventional virus resistance is a robust product of biotechnology because it promises to be more durable than conventional resistance and provides an additional safety factor in that it is not dependent on one mechanism. Resistance can be strengthened through coat protein, antisense, satellite nucleic acid, or interference mechanisms. Although Bacillus thuringiensis (Bt) is the major promising application for selected insect pests on crops such as cotton, there is much variability within this genus that provides the opportunity to exploit a large number of resistance genes for deployment in an effective pest management strategy. There are also alternative genetic modification mechanisms based on completely different genes for insect pest resistance, for example, cpTI, an anti-feedant protein and proteinase inhibitor.

25. Embryo Technology: Technological advances in embryology during the past 20 years have been phenomenal. These innovative advances in biotechnology and embryology already have applications for selected livestock, including embryo transfer, embryonic stem cells, estrus and ovulation synchronization, separation of X-chromosome and Y-chromosome bearing sperm, cryo-preservation of mammalian embryos, in vitro oocyte maturation and fertilization, cloning of mammals by nuclear transplantation. The present decade will see advances related to other techniques such as cloning from somatic sell nuclei, in vitro gametogenesis, blastomere stem cells, transplantation of germline and non-germline cells, successful mammalian artificial chromosomes, and transplantation of chromosomes. Several of these technologies are related to the production of transgenic animals.

26. Transgenic animals: Since the initial insertion of foreign genes in mice, a number of species important to animal husbandry have been made transgenic. These include the chicken, cow, fish, pig, and sheep. The inserted genes for these pioneering efforts have consisted mainly of retroviral genes (used in chickens), and growth regulating genes of several species (used in mammals and fish).

27. So far the practical use of transgenic animals is still limited due to several obstacles to progress such as the lack of identified genes and insertion efficiency; micro-injection is practically the only technology being utilized, but other techniques are being developed that might be utilized in farm animals in the future. Regulation of gene expression and safety issues are other obstacles to the application of this technology, which will however find an important role in animal breeding and veterinary medicine before the end of this decade.

28. Hormones: Animal growth hormone coding genes have been cloned into expression vectors, and introduced into embryos, leading to faster growth and increased milk production. The expression of these genes in bacteria and eukaryotic organisms led to the large-scale production of hormones which are now being released for commercial use. The most studied of them is the bovine somatotropin which produced by recombinant DNA technology and tested in cows. It has resulted in a 41 per cent increase in milk production, without side effects in the quality of the milk. Estimates of the market value of this product amounts to \$US 1 billion corresponding to 100 tons of hormone.

29. Diagnosis: Diagnosis is among the first aspects of medicine to be strongly influenced by modern biotechnology. The use of new assay delivery systems, incorporating monoclonal antibodies and recombinant antigens, have given rise to improvements in sensitivity, specificity, and ease of use. Advances in immuno-assay technology has advanced to permit the capability for brucellosis testing at a rate of 550 samples per hour, by use of a fluorescence-based automated immuno-assay, called Particle Concentration Fluorescence Immuno-assay (PCFIA). In-field brucellosis tests using membrane technology may be performed in less than 10 minutes, with sensitivity equivalent to PCFIA monoclonal antibodies which are particularly useful in competitive assays to measure specific antibody levels in test samples. Such is the case when it is necessary to differentiate a vaccinated animal from an animal infected with wild type virus, pseudo-rabies for example. The utilization of antigens obtained by recombinant DNA, in immuno-assay, makes the cost of these antigens less expensive. The evolution of immuno-diagnostic technologies driven by advances in biotechnology has had and will continue to have a very positive effect on the diagnosis of animal diseases.

30. Vaccines: Based on monoclonal antibodies against pathogens or manufactured through genetic modification, vaccines are in the process of being developed or released against a variety of diseases, including scours, a neo-natal bacterial diarrhoea of calves and piglets estimated to cause the death of several tens of millions of animals of each species annually; viral diarrhoea in calves, bovine adenovirus, porcine adenovirus, porcine infectious rhinotracheitis, Rift Valley fever, and pseudo-rabies disease of pigs, all of which are caused by an Alpha herpes virus which infects the nerve cells and often remains quiescent for long periods before it reverts and causes epidemics; Newcastle disease, which is the most important disease of poultry in the world, and a few parasitic diseases such as coccidiosis in chickens. These are some examples of the impact of the new biotechnologies which also include progressing research and development of vaccines against brucellosis, bovine leucosis, blue tongue, and African horse sickness. Biotechnology also promises for the 1990s a genetically modified vaccine against the foot and mouth disease.

31. Aquaculture and marine: World fishing, while continuing to depend on search, locate, and catch technologies on high seas, is increasingly bringing into practice aquaculture and fish farming at both semi-intensive and intensive scales.

32. A number of developed and developing countries have set up high productivity fish and prawn farming, with yields generally in the range of 10-50 tons per hectare/year in the coastal and inland areas. Several biotechnologies are utilized for hormonal regulation of fecundity, breeding cycles, growth rates, sex selection, all of which has contributed to increased year round harvests and feed conversion ratios. A number of synthetic and biotechnology based peptide analogues are being evaluated as pituitary extract substitutes. Nutritionally balanced new feed compositions not only give high feed conversion ratios but also utilize residues from the agro-fish processing industry. Several successes have been reported in the development of transgenic fish in which the appropriate growth hormone gene has been cloned for higher expression and therefore better growth and feed conversion ratios.

Disease resistance and rapid methods of disease diagnosis are also areas of successful biotechnology applications. Other genes which increase the abiotic tolerance of fish to factors such as the cold temperature of water, have also been used. The factors can be seen to extend the niche boundaries of certain fish.

ENVIRONMENTAL APPLICATIONS

33. Applications of biotechnology have been and are continuing to be developed in various areas of environmental and waste management, particularly land rehabilitation, development of clean technologies, pollution control, and removal of toxic wastes and contaminants.

34. Micro-organisms produced by new technology have much to offer in the coming years by way of the minimization and abatement of environmental pollution. In these applications, organisms will need to be produced that survive and proliferate in the environment, and have their intended effect, but do so in ways that do not disturb the existing ecology.

35. Waste streams generated by virtually all types of human activity place tremendous burdens on the environment. For centuries it has been known that soil micro-organisms have been involved in the degradation processes at landfills, agricultural waste sites, and sewage treatment facilities. Recognition that modern techniques of biotechnology offer unique possibilities to develop organisms that will stabilize a wider variety of possible substrates, such as chlorinated hydrocarbons and enhanced enzymatic activities have led to numerous research programmes. These have been launched by Government, university, and industry to develop such organisms on a large scale. A survey of some of those efforts suggest a number of promising applications, including heavy metal sequestration and degradation of persistent toxic chemicals, such as: TCDD, chloro-phenols, digestion of petroleum products (oil spill dispersion), biomass conversion, and volume reduction of municipal wastes.

36. While treatment of waste is an important application, the most promising areas of application of new organisms is in clean technology, applied directly to manufacturing processes. Such modifications are simpler to manage and deal with potential waste streams at the point of origin. In addition, such waste minimization procedures have the advantage that the organisms used can be confined and therefore present less of a burden in terms of the assessment of possible risks particularly to the environment. Examples include deamination of residual amino-naphthalenes in the dye industry; denitration of cyanide-producing industrial processes; partial detoxification of certain hazardous chlorinated by-products of pesticide manufacture; digestion of lignins in pulp and paper industry (also technology for less water and chlorine); and use of new organisms for development of cleaner technologies in distillery and tannery related facilities.

37. Energy and mining: There are a number of possible future application of biotechnology with respect to energy and mining. Micro-organisms have been used in the past for the recovery of metals from ore, albeit in relatively restricted circumstances. It is possible that r-DNA techniques could be used

to develop organisms with greater tolerance to acidic or saline conditions, or increased ability to survive high or low temperatures, leading to a greater capacity for leaching a number of metals in the future.

38. Much of the world's oil reserves are either trapped in rock formations or are too viscous to pump. It is possible that in the future, microbial bio-polymers, perhaps produced by r-DNA techniques, will be used as emulsifiers to aid oil recovery rates.

39. The conversion of biomass for energy purposes may also be an important aspect of biotechnology in the future. Several countries already have launched major alcohol projects. A switch to biomass-based processes, however, will be determined largely by comparative costs. Improvement in the types and range of organisms available for fermentation, as well as distillation technology, will also be important.

40. Production of biomass to exploit alternative strategies for generating energy from a renewable resource, as opposed to fossil fuels, can be an important contribution of biotechnology. The development of crops resistant to abiotic diseases on marginal land, for example, drought, heavy metal toxicity or mineral deficiencies and toxicities will allow land that is currently non-cultivable to be brought into production and increase incomes of the rural poor. Similarly, development of crops that will provide and reverse land degradation can be major long-term benefits from biotechnology.

41. Industry: While almost all products of biotechnology will have to be produced using industrial scale production technologies, mention should also be made of products that are of high value/low volume and high volume/low value. Considerable success has been achieved in the production of ethanol and butanol from carbohydrates and cellulosic residues. Other products include single cell protein, amino acids, antibiotics, and enzymes steroids. Production of microbial polymers for the chemical and petroleum industry has also made much progress. In the area of bio-conversion, useful by-products from urban industrial and agricultural residues include methane and animal feed. In a more recent development, a number of new bio-sensors using enzymes or antibodies are leading to the detection of metabolic products in body fluids and various effluents in a highly sensitive and specific manner. Bio-sensors for detecting blood glucose are already on the market.

42. Forestry: Maintenance, preservation, and improvement of forest tree species require longer-term investment than for comparative programmes in annual and perennial crops. To date, forestry has not benefitted significantly from the application of biotechnology, but stands to gain more future benefits. For example, some of the tropical tree species that contribute to biodiversity in both natural and commercial forests in developing countries do not lend themselves for easy propagation by seeds. Tissue culture can overcome some of these disadvantages, contribute to the maintenance of genetic resources, and help accelerate natural and commercial reforestation programmes.

43. The use of new biological pesticides may control large-scale epidemics and infection in extensive forests, contributing to more sustainable forest

protection and less dependency on traditional chemical pesticides. Similarly, use of biotechnology to develop tree species to withstand acid-rain and other industrial pollutants could relieve significant pollution problems in the industrialized and developing world.

APPLICATION SELECTION

44. Information for assessing the feasibility and choice of biotechnology applications: Investments in biotechnology depend on in-depth information on variables which define opportunities and comparative advantages of specific products and technologies. Listed below are examples of the information needed for sound investment and application.

- a. Basic scientific information (molecular and other basic scientific data related to the organism, gene, vector, insert, etc.);
- b. Availability of germ plasm (genes, gene pool, host organisms);
- c. Adaptation of local conditions and needs;
- d. Skills and manpower (available vs. training needs, level of qualification and critical mass of personnel required for the specific application);
- e. Management infrastructure available (description of required facilities);
- f. Environmental or site-related information or databank;
- g. Competitive technologies/product development and alternative choices (i.e. who is working on the application being considered; who does it best under the local circumstances; what is the variation in cost among alternatives; what are the cost advantages and substitutions);
- h. Stage of development (e.g., research, safety trials, performance trials, commercialized);
- i. Funding arrangement and cost (investments needed, funding opportunities, consortium);
- j. Market size (local, regional, and global application, share of intended market, value);
- k. Beneficiaries and social consequences (information on consumers users intended to handle the product or technology);
- l. Proprietary rights and civil repatriation (description of the legal intellectual proprietary rights present in the country, as well as specific currency requirements);
- m. Potential environmental and health impacts;
- n. Environmental or health concerns of alternatives or current products;

- o. Technology: Optimization of the scale of application (complex industrial, small- and medium-size, cottage, backyard).

BIOTECHNOLOGY AND SUSTAINABLE DEVELOPMENT: PROMOTION, TRANSFER AND ENABLING MECHANISMS

45. New biotechnology techniques, used in conjunction with traditional methods, offers countries a unique opportunity to address national priorities on sustainable development and the environment in effective ways. Sophisticated biotechnology tools and products provide an impressive array of possible applications to enable important national development to be addressed. The process of transferring these technologies from industrialized countries to developing countries allows national capacity in the latter to be developed in a sustainable mode. More specifically, national goals of alleviating poverty through increased availability of food and provision of a better quality of life can be achieved.

46. Similarly, development of biotechnology for increased productivity of food, feed, and fibre in the rural areas will provide increased employment opportunities for the rural poor and better incomes for rural communities. Biotechnology is no different to any other technology in that challenging issues have to be overcome before the gains from adopting the technology can be realized. They can be overcome if addressed on a case-by-case basis.

47. Development Status of Recipient Country: Most developing countries lack the necessary physical facilities and trained staff to participate meaningfully as a partner in joint ventures. Similar difficulties will arise in organizing an effective distribution and implementation system for biotechnology products requiring specialized technical support. Fortunately, these constraints do not apply to the same extent when the biotechnology product is a gene controlling a beneficial trait which has been incorporated into germ plasm. For example, seeds for a crop containing a new disease resistance gene is planted in the same way as its traditional counterpart.

48. A very important issue is the trust and confidence of political leaders, decision makers, and farmers with regard to biotechnology products. The decision to accept these products must be taken within the broader context of the long-term consequences of applying biotechnology. It must be demonstrated at the field level, under the prevailing agricultural and environmental conditions, that significant increases in productivity result from the application of high value biotechnology products.

49. The decision of developing countries to accept or reject products of biotechnology has both political and policy implications and could be taken within the broader context of the long-term consequences. These include opportunities for developing countries to improve the quality of crops to develop export markets, as well as satisfying local and current demands.

50. Conversely, industrialized countries can modify crops with biotechnology to substitute traditionally imported crops from the developing countries. There is little doubt that in the long term such quality changes will become

possible with biotechnology, and hence prudent decision-making in the short term could anticipate long-term developments. Failure to make the right decisions at the initial stage could lead to a greater disparity between industrialized and developing countries if the latter cannot access technological developments that lead to increased productivity and more competitive marketable products. An appropriate strategy for both developing and industrialized countries could be to identify and select those biotechnologies and products which will bring the best comparative advantages to both sides on a long-term basis, based on adequate marketing criteria.

51. Regulatory issues: Experiences in industrialized countries suggest that regulatory issues evolve as a significant issue when a biotechnology is being tested. Credible safety regulation is prerequisite for major private investments in biotechnology.

52. Currently there is no common approach to regulation in different countries and regions of the world. The establishment of a harmonized approach to regulation could promote the development of this technology by allowing research and performance trials to be conducted and products to be used globally without widely differing requirements being imposed on the researcher or industry. Such harmonization would also aid the exchange of information.

53. An immediate way to assure the transfer of a product from an industrialized country, which may require testing in a developing country, is to perform tests based on the regulations available in industrialized countries for the specific product. Transfer and testing should also be dealt with a case-by-case basis, until experience accumulates in developing countries in this area. Even when such an approach is considered, the country in which the product would be tested should be informed first.

54. Private Sector Investments in Biotechnology: In the past, developing countries have been able to access traditional non-proprietary technology relatively freely and easily from the public sector. However, the advent of biotechnology has resulted in the private sector being the major investor, estimated to spend approximately \$US 8 billion, equivalent to 75 per cent of the annual \$US 11 billion global research and development budget in biotechnology. Accordingly the challenge is to develop institutional mechanisms that will allow the transfer or acquisition of proprietary biotechnology applications from the developed countries particularly the private sector to the benefit of developing countries.

55. Intellectual Property Rights (IPR): IPR protection is an important promotional requirement for adequate investment in research and development and its large-scale commercialization by the inventor. While developing countries have generally adopted a patent rights policy that serves their best national interests, owners of intellectual properties need assurance that such policies can protect their commercial interests. It has been argued that in the area of new plant varieties of higher economic potential, adequate plant varietal protection rights to the breeder may have to be provided without affecting the rights of the farmers.

56. Germ plasm as Resource for Biotechnology and Development: Developing and developed countries could combine their respective genetic and technological resources in order to realize the mutual benefits of biotechnology. Efforts to establish equitable reciprocity should receive high priority. The conservation and rational utilization of genetic resources can only result from an international cooperative effort. As gene functions are gradually understood, genebanks established, and biotechnology for genetic resources conservation and utilization developed, the access to genetic resources and relevant technologies will be facilitated.
57. The challenge is to elaborate an integrated programme which will use biotechnology to ensure development, based on an adequate mechanisms of germ plasm conservation and utilization and conditions which are safe for human health and the environment.
58. The implementation of such a programme will have to consider two essential components; a clear definition of priorities to meet a typical "market oriented" approach in biotechnology and the magnitude of the financial investment needed for safe procedures of environment conservation and the special needs of developing countries.
59. Enabling Mechanisms: There is an evident need for efforts to accelerate the transfer of biotechnology applications and related activities to developing countries.
60. It is estimated that 75 per cent of the current investments in research and development are made by the private sector. It therefore follows that the majority of the superior technologies in the future will be proprietary. Transfer of selected proprietary technologies such as vaccines and non-conventional virus resistant plants has been achieved. Much more effort is needed to supplement the programmes that are currently operational if the significant biotechnology needs of developing countries are to be met.
61. The creation of a Biotechnology Consortium for Development (BCD), as a joint venture among the respective shareholders from developing countries, bilateral/multilateral agencies, and the private sector, may provide new mechanisms for developing countries to accelerate the acquisition of both non-proprietary and proprietary technologies.
62. In practice, the effective operation of such a consortium would require the national priorities of the developing country concerned to be addressed on a case-by-case basis, so that capital investments could be secured and mobilized in relation to specific project needs. Capitalization of such a mechanism would require detailed pre-investment feasibility studies to evaluate priority needs of developing countries, identify appropriate technology for transfer, and identify financial and material benefits for all partners.

PART II

SAFETY IN BIOTECHNOLOGY: RISK ASSESSMENT AND RISK MANAGEMENT

INTRODUCTION

63. Biotechnology, like other technologies, is a tool aimed at developing specific applications. As with the development of every technology therefore, safety in biotechnology should be an integral part of biotechnological development. Decision makers require information assessments of the potential benefits as well as of the potential adverse effects. Only if there is both adequate risk assessment and risk management can the community at large benefit from the potential of biotechnology. More than a decade of experience with contained industrial use clearly demonstrates that safety in biotechnology can be achieved by applying adequate risk assessment and management. This provides a sound basis on which to build for the future.

64. This part of the integrated programme on biotechnology builds upon and further refines internationally accepted principles and methodologies of safety in biotechnology. It is based upon two elements:

- a. The recognition that there are already many internationally developed methodologies for safety in biotechnology and that duplication of effort should be avoided as much as possible.
- b. The extent to which safety methodologies and procedures can be conducive to the global environmentally sound management of biotechnology, depends, among other things, on the level of international harmonization of these methodologies and procedures, and their internationalization and implementation.

65. The introduction of the new molecular technologies in biotechnology in 1972 triggered a discussion on safety in biotechnology. This discussion resulted in a large number of national and international safety recommendations, guidelines and legislation, including:

- a. OECD: Recombinant DNA Safety Considerations;
- b. European Community: Directive on the contained use of genetically modified micro-organisms. Directive on the deliberate release into the environment of genetically modified organisms.

COMMON PRINCIPLES

66. A review of existing guidelines, recommendations, studies and legislation on safety in biotechnology highlights five fundamental principles:

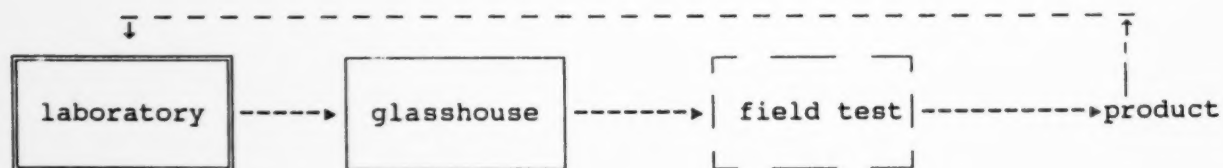
67. A primary consideration of the organism: Organisms have been used for various purposes for a long time, including the introduction of non-indigenous organisms. Awareness of the need for environmental protection has led to an appreciation of the need to address potential effects of non-indigenous organisms on human health and the environment.

68. The increasing use of modern biological techniques of genetic modification has enabled significant new development to take place in biotechnology. As a result, most, if not all, of the existing documents on safety in biotechnology show various degrees, a focus on genetically modified organisms (GMOs). It is generally recognized that the techniques of genetic modification are neither inherently risky nor inherently safe. The potential risks depend however on the organism used, the conditions under which it is used, and the receiving environment, or potential receiving environment. The reason for focusing on GMOs is based on the lack of empirical data on impacts of these organisms with modified traits, together with the fact that impacts of organisms on the environment may be irreversible due to reproduction and dispersal.

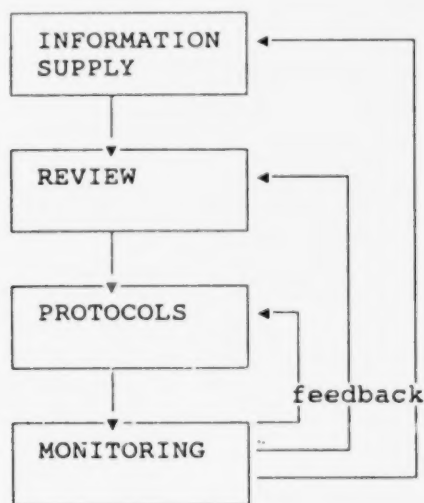
69. None the less, since potential adverse effects depend on the organism, safety considerations are similar both for the non-indigenous and genetically modified organisms.

70. A general principle for safety in biotechnology (the step-by-step principle): This principle requires that the development of the application of an organism should be conducted step by step, each new step building on the experience from the previous step. This means that the safety of an organism and its application is reviewed in a step wise manner, the steps needed depending on the assessment of the risks. In general, for contained uses, this means development from laboratory experiments to small-scale and then larger-scale operations; and for releases, development from laboratory experiments to experiments in the glasshouse, microcosm, etc., and then to trials in the open environment (field tests, small and large scale) and appropriate tests prior to the placing of the final product on the market, after which product assessment such as efficacy and quality is applied.

71. For releases, therefore, in each next step, the containment or confinement is gradually reduced, but only if such a step is justified on the basis of the results of the previous steps:



72. Complementary aspects of safety: risk assessment and risk management: Most of the approaches to safety in biotechnology comprise four steps, of which the first two constitute the risk assessment, and the last two the risk management, i.e. supply of information; review prior to experiment; description of safety procedures and protocols; monitoring before, during, and after the application.



73. A general distinction between contained use and release: The contained use of organisms is generally regarded as any use in which the contact of organisms with the environment is limited by physical barriers and biological barriers. Examples of contained uses include laboratory facilities and fermenters. Now, after 20 years of experience with small-scale contained use of GMOs and, in some countries, more than a decade of large-scale use, classification into risk management categories of an organism and its application have been used as a basis for categorizing safety procedures.

74. Release is generally considered to be any non-contained use. Sufficient data are not available to permit any classification of releases of GMOs. For this reason, there should be a case-by-case review of the release of GMOs. The release itself constitutes a development from contained use according to the step by step principle.

75. A framework for safety in biotechnology: It is generally recognized that the different elements of safety in biotechnology can not be applied in a random manner. A framework, be it in the form of guidelines or in the form of regulations, is a prerequisite for adequate risk assessment and risk management. The framework could also take recognition of the fact that GMOs, like all organisms, are not stopped by national boundaries.

CURRENT PRACTICES FOR RISK ASSESSMENT

76. One of the common elements is the relationship between risk assessment and risk management. In order to be able to make an assessment of the risk associated with a proposed contained use or release, it is necessary to address, on the basis of available information, a number of questions.

Information requirements for contained use

77. Overview of existing information requirements: There are a number of international and national documents that are relevant: in particular, OECD Recombinant DNA Safety Considerations, 1986, EEC Directive on the Contained Use of Genetically Modified Micro-organisms (90/219/EEC), ILO Study on Safety in Biotechnology, national guidelines.

78. Common elements: All documents referred to above recognize that not all information will be relevant in a particular case. The common elements are outlined below, paragraphs 79 to 83 reflecting characteristics that are related to the organism, and paragraphs 84 and 85 characteristics related to the contained use.

79. Characteristics of the recipient/parental organism: The relevant physiological and biological characteristics of the recipient or parental organisms are to be considered. These include:

- a. The identity of the organism;
- b. The pathogenicity and toxicity to humans and to other organisms;
- c. The ability of the recipient/parental organism to survive, multiply and disseminate in the environment;
- d. The stability of relevant genetic traits and information on indigenous vectors;
- e. The means and potential for transfer of genetic traits to other organisms.

80. Characteristics of the donor organism: The relevant characteristics of the donor include, in particular, the pathogenicity and toxicity.

81. Characteristics of the vector: Information relevant to the vector:

- a. The nature, source and method of construction of the vector;
- b. The amount of vector remaining in the modified organism and the characterization of the structure of such material;
- c. The frequency of mobilization and/or genetic transfer capability.

82. Characteristics of the insert: The information requirements are:

- a. Characterization of the nature and function of the inserted nucleic acid (i.e. the inserted material and residual vector);

- b. The methods used to construct and introduce the material into the recipient organism, the rate and level of expression of the introduced genetic material, and the activity of the expressed protein (in the recipient organism).

83. Characteristics of the genetically modified organism: The modified and the recipient organism need to be compared in terms of their biological and physiological characteristics. These include:

- a. Information relating to the health of humans and other organisms (pathogenicity, toxicity, allergenicity, etc.);
- b. Factors affecting the survival, reproduction and dissemination of the GMOs in the environment, should an accidental release of the GMOs occur;
- c. The stability of the organism in terms of genetic traits, its capability to transfer genetic material and routes of potential dissemination;
- d. Methods for the detection, identification and monitoring of the organism and for detecting transfer of the donated DNA to other organisms;
- e. The capacity of the GMOs to colonize humans (or animals/plants, if appropriate) as a host.

84. Characterization of the contained use: The information requirements need to embrace not only the organism itself, as outlined above, but also the particular operation. The containment for any GMOs needs to be appropriate to the risk imposed by that organism and the intended type and scale of operation; containment levels are considered below.

85. Characterization of safety procedures: The rigour of procedures to be adopted for the safe operation of a contained use reflects the risk associated with any particular application of a GMO. Information for the human and environmental risk assessment should include modification measures, work practices, personal protection, waste treatment and monitoring to permit the appropriate setting of safety requirements, the latter being closely linked to the risk management.

Information requirements for release

86. Overview of existing information requirements: Many of the documents presented in paragraph 77 also contain sections dealing with information requirements for releases. In addition, a number of documents deal specifically with information requirements for releases. These include:

- a. OECD Recombinant DNA Safety Considerations;
- b. EC Directive on the deliberate release into the environment of genetically modified organisms;
- c. OECD report: Good Developmental Principles (GDP).

- d. Australian Recombinant DNA Monitoring Committee: procedures for Assessment of the Planned Release of r-DNA Organisms;
- e. US Ecological Society: The Planned Introduction of Genetically Modified Organisms; Ecological Considerations and Recommendations;
- f. US Office of Technology Assessment report: Field Testing Engineered Organisms: Genetic and Ecological Issues;
- g. NRC report: Field testing of Genetically Modified Organisms: Framework for decisions;
- h. UK Royal Commission on Environmental Pollution: The Deliberate Release of Genetically Engineered Organisms to the Environment;
- i. US Department of Agriculture Report: Guidelines for Research with Genetically Modified Organisms Outside Contained Facilities;
- j. UK ACGM/HSE Note 3: The Intentional Introduction of Genetically Manipulated Organisms into the Environment;

87. Common elements: As with contained uses, one common element is that the documents give recognition to the fact that not in every case is all information relevant. Although the documents mentioned above vary in the level of detail, they all require information on the following elements:

- a. Characteristics of the recipient or parental organisms;
- b. Characteristics of the donor organism;
- c. Characteristics of the vector remaining in the organism;
- d. Characteristics of the insert;
- e. Characteristics of the GMO;
- f. Characteristics of the release;
- g. Characteristics of the receiving environment;

The details of (a) to (e) are as outlined in paragraphs 79 to 83. In addition:

88. Characteristics of the release: The level of detail required for each individual consideration is likely to vary according to the nature of the proposed activity. The information required includes:

- a. The size and location of the release;
- b. The method of release and quantities of organisms to be released;

- c. The subsequent treatment of the site and plans for waste management and emergency response;
- d. Details of any previous release of the organism.

89. Characteristics of the receiving environment: The information required includes:

- a. Methods of site disturbance or cultivation;
- b. The physical proximity of the site to people and/or other significant biota;
- c. The geographical location of the site, including specific features of the receiving environment, such as climate, temperature, geological and pedological characteristics;
- d. Flora and fauna and the ecosystems that could be affected by the release;
- e. Details of any previous release at the site.

Databases

90. Overview of existing databases: Computerized and other forms of databases are essential elements of a systematic approach to safety in biotechnology and to the process of internationalization discussed below. A number of databases have been established or are in the final stages of preparation. Others are under consideration or in early stages of development. The databases relate to regulation, introductions or releases, microbiology, molecular biology, cell lines and hybridomas, sequence data, bibliographic and general biotechnology information. The major databases are: OECD's Bio-track on the Use and Release of Organisms; culture collection catalogues (United States, European countries, Japan, Brazil) including the World Data Centre's Directory to Culture Collections of Micro-organisms; national and regional microbial strain databases (MiCIS, MINE in Europe); Hybridoma Data Base, Immunoclone Database, Interlab Animal Cell Database; sequences databases (EMBL, Seqnet, Can/Snd, Gen Bank); botanic databases (ILDIS; taxonomic databases (Biosis, ICECC); plasmids/vectors/gene libraries (NIH Repository of Human DNA Probes); bibliographic (DataStar, Dialogue); general biotechnology (BioIndustry Association databases, BIKE, BIOREP); Biotechnology Information Knot for Europe of GBF in Germany. Many of these are linked through the internationally sponsored information and communications Microbial Strain data Network (MSDN).

91. In addition a database containing information on national and international safety standards, training materials, studies and other publications concerning safety in the workplace in biotechnology is held in the International Occupational Safety and Health Information centre (CIS) of the ILO.

92. Common elements: Most of the databases listed were not developed specifically for aiding the risk assessment and risk management of organisms,

but they can undoubtedly provide data useful both for individual assessments of new organisms and for general development of methods and background data on the ecology of release sites. The contents of these databases are diverse and have few common elements. Common elements that are contained in databases developed specifically for information on releases (e.g. BIOTRACK) include:

- a. Parental/host organism;
- b. Donor organisms;
- c. Insert;
- d. Vector;
- e. Release characteristics.

Assessment of risks in contained use

93. Overview of existing documents: The documents referred to in paragraph 77 are all of relevance here.

94. Common elements: Case-by-case assessment of the risk associated with the organism is required in order to assign an appropriate containment category to the operation. In assessing the risk, there are four central questions that need to be addressed:

- a. What is the likelihood of the organism escaping in sufficient quantities to have an adverse environmental effect on human health and the environment, and if so, what would this effect be?
- b. What capacity has the organism to transfer the genetically modified material to other organisms in the event of escape from the contained use?
- c. In the event of an escape could the possible effect be mitigated?

95. This requires assessment of the information such as the survivability (and hence any built-in biological barriers), pathogenicity, reproduction and dispersal, etc. of the organism. In addition, account also needs to be taken of the scale of the operation, available processing and disposal methods, including the equipment to be used, and the nature of the product.

Assessment of risks releases

96. Overview of existing material: Most of the documents mentioned in paragraph 77 are also relevant here.

97. Common elements: Three fundamental questions need to be addressed:

- a. Can the GMOs or its descendants, as a result of the genetic modification, have an adverse effect on human health and the environment, and if so, what would the effect be?

- b. Can the genetically modified material be transferred to other organisms which, as a result, could have an adverse effect on human health and the environment, and if so, what would the effect be?

98. The information required to assess these questions is the information described in paragraphs 87 to 89 in combination with the results of pre-release tests, carried out in laboratories, glasshouses, etc.

RISK MANAGEMENT: CONDITIONS FOR SAFETY

99. Having identified and assessed the risk associated with any particular application of an organism, the next step is to consider how that risk can be minimized and is best managed. It is important to note that the continuous review of all the management procedures is an integral part of the overall management process.

Safety conditions for contained use

100. Overview of existing material: The same documents are relevant to paragraphs 79 to 83. There are also many national guidelines. Although most of the national guidelines and regulations include references to emergency planning and response, there are few documents dealing specifically with this. The ILO Code of Practice on the Prevention of Major Industrial Accidents to all industries, and the principles contained in this document are relevant. Also the EC directives on GMOs contain administrative procedures to be followed and information to be supplied in the event of accidents. The Seveso directive is also relevant.

101. Common Elements: The safety of contained uses depends on the organism used and on the adoption of containment measures which are appropriate to the level of risk. Categories of containment reflect the different potential for organisms to cause harm when used in particular applications.

102. Scale: The scale of an operation must be taken into account in assessing, and therefore managing, risk. Small-scale laboratory-based experiments are considered to be different from large-scale industrial practices. Practices which are appropriate to small scale may not be so to large-scale uses (and vice versa).

103. Containment measures: Adequate protection for human health and the environment is provided by applying fundamental principles of good practice to ensure the lowest practicable exposure; controlled measures and equipment; monitoring for escape of organisms; training of personnel; waste treatment and provision for local safety procedures.

104. Containment levels: Genetically modified micro-organisms considered to be relatively low-risk (i.e. innocuous to human health and the environment) will require fewer controls and containment, such as the Good Industrial Large-Scale Practice (GILSP) developed by the OECD and the EEC's Group I organisms. Alternatively, medium or high risk GMOs will certainly require far more stringent controls and containment.

105. Containment levels could be periodically reviewed by the user to take into account new scientific or technical knowledge which may have an impact on the risk management, including, for example, the treatment and disposal of wastes.

106. Waste Treatment: Requirements for treatment of wastes from contained uses depend on the organism used. Environmental factors identified in the risk assessment clearly are key to designing appropriate procedures for waste management.

107. Contingency planning and mitigation procedures: For certain types of contains use, i.e those of higher risk, contingency plans are required. These comprise the submission of emergency response proposals prior to the application; notification to relevant local authorities and parties and those members of the public who could be affected; and mitigation procedures to be followed in the event of an accident occurring.

Safety conditions for release into the environment

108. Overview of existing material: Due to the case by case assessment to be applied, the description of safety conditions has in most cases also been developed on a case-by-case basis. However, attention has already been given to the need to categorize safety conditions for releases. The documents referred to in paragraph 77 are relevant here, and in particular:

- a. OECD report: Good Developmental Principles (GDP);
- b. US Ecological Society: The Planned Introduction of Genetically Modified Organisms; Ecological Considerations and Recommendations;
- c. Australian Recombinant DNA Monitoring Committee: Procedures for Assessment of the Planned Release of r-DNA Organisms.

109. Common elements: As mentioned above, procedures for safety on releases are generally established on a case by case basis. However, a few common principles emerge from a review of the guidelines and documents:

- a. The step-by-step principle could continue to apply. This means that the step from glasshouse or microcosm to field test is not the final step, but that the field tests themselves could follow an approach of gradually relaxing constraints and expanding the size of a test;
- b. For the experimental stage, the design of the trial could permit limitation of reproductive capacity, competitive ability, transfer of introduced genetic material and dispersal beyond the test site, and appropriate monitoring of effects.

110. The documents also reflect the fact that once organisms have been released, they cannot always be recalled. Contingency plans and mitigation procedures are required:

- a. For the event that the assessment of risks associated with the release proves not to be wholly correct;
- b. For the event that unanticipated effects arise as a result of the release.

111. In either of these cases, it may be necessary to change the risk management practices in order to mitigate the effects, or it may prove necessary to destroy the organism, and decontaminate the site. As with contained use, contingency plans and mitigation procedures have to be prepared prior to the release and there has to be notification to relevant authorities and the public.

Environmental Monitoring

112. Overview of existing material: Most of the national guidelines include some monitoring requirements, which focus mainly on tracking a specific organism over a period of time. Most guidelines elaborate on detection and identification techniques.

113. The OECD initiated a discussion on monitoring in a broader sense, by organizing an international workshop in 1990. This resulted in the OECD draft report "Monitoring of Genetically Modified Organisms Released to the Environment".

114. Common elements: A review of the national and international guidelines and the OECD report reveals several general principles:

- a. Monitoring is absolutely imperative for the safe development of GMOs;
- b. Monitoring is an essential and integral part of the step by step procedure. Appropriate monitoring at each step is dependent upon risk assessment. Without monitoring in fact, no next step should be taken. Monitoring at this stage serves to check, for example, pre-release assumptions on survivability, dispersal and gene transfer. This form of monitoring focuses mainly on tracking the GMO and the inserted gene. Depending on the monitoring objective, different detection techniques can be applied. Criteria for choosing the most adequate technique are: sensitivity, specificity, availability, ease of use, reproducibility and reliability, and cost;
- c. Monitoring for adverse effects on human health and the environment.

Independent review for compliance

115. Inspections: The term inspection is used to describe an independent review of the facilities (contained use) and sites (release); the practices and procedures followed; and confirmation of compliance with the required risk management conditions. The last two are applicable to both contained use and release. Inspection is not continuous, but takes place at intervals.

116. Overview of existing material: An international document relevant to inspection from a worker safety aspect is the ILO Convention No. 81 on Inspection and the ILO Study on Safety in the Use of Biotechnology. A number of the national guidelines make some reference to inspections.

117. Common elements: In the main, existing national institutions responsible for inspection cover mainly those branches of industry in which there are publicly recognized hazardous conditions attached to the work. The introduction of new technologies is not always followed by the creation of new specialist inspectorates which are able to monitor compliance and inspect, but rather lead to existing inspectorates being required to expand their skills. There is not always adequate worker collaboration during inspection.

118. In this document, the term inspection is used to mean the review by an independent institution of organizational approaches to the facilities provided, and the practices and procedures followed, both for contained use and releases.

INTERNATIONAL COOPERATION ON SAFETY IN BIOTECHNOLOGY

119. The aim of this part of the integrated programme is to enable biotechnology to be developed and applied beneficially throughout the world, without the unintended side effects that have diminished the benefits associated with other new technologies in the past. Realization of the potential benefits of the technology is dependent on appropriate safeguards to prevent damage to human health and the environment.

120. International cooperation will be needed in developing the areas of further work which extend beyond the common elements set out above for the establishment of a set of internationally accepted guidelines on methodologies for the assessment of risks associated with biotechnology and procedures for managing those risks; and the setting up of mechanisms for international information exchange. Wherever possible this could take place by augmenting and strengthening ongoing activities, such as the activities of the OECD, the EEC, the UNIDO/UNEP/WHO/FAO informal working group, etc.

121. This will necessarily take some time to be attained; but by combining a number of short-term mechanisms and intermediate steps, steady progress towards, and achievement of, that goal would be ensured.

IMMEDIATE ACTION TO AID SAFE DEVELOPMENT OF BIOTECHNOLOGY

122. The initiation of a programme of international cooperation and a regional approach, and the setting up of mechanisms for the dissemination of information and provision of assistance, could be readily put into place in the short term. This would contribute significantly to the safe development of biotechnology.

123. International cooperation: Progress in the development of biotechnology will be accelerated if there is sustained and comprehensive international cooperation. The need is heightened because of the ability of organisms to cross national boundaries.

124. Cooperation can be achieved by the establishment of information exchange between Governments, regions, industry, research institutions, and international organizations, as described in paragraph 128 below. It can also be aided by the establishment of agreed approaches and procedures and be furthered by providing information for the public. The disclosure of information to the public is a key area, in which both national and international organizations have a major role to play.

125. Regional approach: Very few countries in the world are able to establish a comprehensive mechanism for risk assessment and management without enlisting the support of other countries and international organizations. The adoption of a regional approach as an instrument for the international cooperation referred to above will be of value. Such an approach means that a number of countries may agree to form a group, within which expertise may be shared by arranging meetings, reciprocal visits, and exchanges of experts, etc. These regional groups could be linked together in the form of networks. Two examples of regional groups are the Latin American Study Group on the New Biotechnologies, and the European Community. The legal status of the EEC provides the possibility for harmonized legislation at the regional level, and such binding legislation was adopted in 1990 both for the contained use and release of genetically modified organisms. Possibilities are provided under this legislation for cooperation and exchange of information and experience between the competent authorities.

126. The basis for these two regional groups is largely geographical, but other regional groups could be established on a different basis, such as language or regional cooperation, or ecological or agricultural similarities. Member States may wish to indicate their support for this approach, and putting forward proposals for the composition of such regional groups.

127. The early setting up of a number of regional groups throughout the world would foster the international cooperation needed in this area.

128. Mechanisms for dissemination of information and provision of advice: An integral part of cooperation is the exchange of information. In the short term, information could be made available to those interested by setting up the mechanisms outlined below:

- a. The nomination by countries of a national authority which could serve as a contact point for other national authorities and international bodies, and could also provide links to regional groups and established safety committees which advise on genetic modification and releases of organisms to the environment;
- b. the establishment of an international coordination point which could, if requested, link national authorities; provide advice directly or indicate where advice could be obtained about a particular organism, and about risk assessment and management; notify the traffic in certain organisms between countries and supply the information necessary for the receiving country to be able to conduct a risk assessment.

129. Paragraphs 65 to 118 highlighted the currently limited experience on the impact of organisms released to the environment and the need for case-by-case review. The mechanisms described in this part could be extended to include the notification of an intended export of an organism intended for release. Notification by the exporting country could be made both to the international coordination point and to the importing country. The latter could be asked for a decision as to whether or not the export should go ahead. Such a flexible approach to notification both to the importing country and the international coordination point would readily allow for the wide dissemination of information as well as for the establishment of bilateral communication, thereby furthering international cooperation.

INTERMEDIATE STEPS TOWARDS AN INTERNATIONALLY HARMONIZED SET OF PROCEDURES FOR ASSESSING AND MANAGING BIOTECHNOLOGY RISKS

130. Making information available: In order to guard against duplication of work, and to provide a useful coordinated supply of information for the national authorities and other bodies, the international coordination point would be responsible for collecting all existing national and international guidelines relating to risk assessment and management, and relevant recommendations and legislation. There is an important role to be played here by international databases.

131. Adaptation of material to regional needs and circumstances: The collected material would need to be translated and adapted, as required, to the specific ecological and institutional circumstances of the different regions. This would require close cooperation between the national and regional groups involved and the international coordination point. Specific attention should be given to vulnerable ecosystems.

132. Comprehensive international risk assessment and management procedures: The collaborative work between the regional groups and the international coordination point in those areas which have been identified earlier as requiring further work could result in a set of guidelines on risk assessment and management applicable to all regions throughout the world. This set of guidelines could be one of the cornerstones of the integrated programme on environmentally sound management of biotechnology.

133. Information exchange and international notification procedures: The mechanisms described in paragraph 128 could serve to make available to all countries the documents material emerging from the activities set out in the previous paragraphs.

134. Education and training: The environmentally sound management can only be achieved if there is adequate provision for education and training. This is particularly so for developing countries, which need to attain the critical mass of scientists and technologists needed for accelerating meaningful research and development in biotechnology and related fields. A whole spectrum of education and training activities relating to biotechnology safety needs to be planned and implemented.

AREAS FOR FURTHER WORK

135. Information requirements for contained use: Although the principles set out in this report provide a sound basis for safety in biotechnology, there are many areas which require further attention before a comprehensive set of internationally acceptable procedures for risk assessment and management can be put in place.

136. Further work is required to harmonize approaches to the categorization of risk imposed by different GMOs and the corresponding level of containment, appropriate to the scale. This will involve agreement on what constitutes a particular level of risk, and what containment could be imposed to make that risk internationally acceptable. In addition, there will be a need to categorize vectors and inserts, etc.

137. Although a number of national guidelines address the appropriate containment of genetically modified organisms that are not micro-organisms, most international guidelines to date are biased towards the contained use of genetically modified micro-organisms. There will be an increasing need for international harmonization on containment for all types of organisms as biotechnology develops.

138. Information requirements for release: Further work is necessary on the impact of certain releases in a wide range of different environments. To underpin this, work on the characterization of different ecosystems and their interaction, and the impacts of released organisms on ecosystems is necessary in order to be able better to assess potential environmental impacts.

139. Databases: The OECD BIOTRACK Pointer System includes some of the data commonly required about organisms, release parameters, risk assessments and monitoring. A number of national authorities provide the information to OECD which then summarize it. These and other national authorities have or are developing their own databases which contain more information.

140. There is a clear need for an integrated international information network or system covering both non-modified and genetically modified organisms, genes, vectors, and inserts, and results related to risk assessment and management. This requires a minimum package of information on applications which could be freely available to the public. There could also be provision for data on national regulations, guidelines and requirements, human resources available for consultation on safety issues, ongoing research projects, including research on safety issues, and products in the market place.

141. The preferred model would be a distributed and flexible network linking both existing resources and new databases; the separate data elements could be linked by gateways where appropriate and usage could be facilitated by the development of new interfaces. Data could be made freely available without restriction as far as possible. Regional help desks and training could be an integral part of this work.

142. Procedures for assessing risks in contained use: Procedures could be developed for assessing the risks associated with contained uses of organisms other than micro-organisms. There is also a need to harmonize approaches to the types of containment appropriate to different organisms and modifications.

143. Procedures for assessing risks of releases: Risk assessment of releases has to be conducted on a case by case bases, due to the insufficient data. A major area of further work would involve gathering comparable data and disseminating them in a efficient manner. It is also necessary to promote further research to provide data not yet available on a variety of organisms, ecosystems and the likely interactions and impacts.

144. There are two particularly important areas for further work are. The first is the assessment of the impact on different ecological environments and processes; organisms may have different impacts on different ecological environments. In this context, it is important to realize that most of the cultivated crops subject to genetic modifications originate from tropical and subtropical areas in which the impact is likely to be different from the impact in temperate environments.

145. The second important area for further work is the assessment of potential long-term effects which would involve continuous environmental monitoring, and thereby provide a sound basis for risk assessment and the development of appropriate management procedures. Most of the risk assessment procedures described to date offer adequate assessment of the expected short-term impacts. Work on impact assessment could focus in addition on the possible long-term effects, including assessment of synergistic and pleiotropic effects, and possible secondary effects. There should be equal attention given to both short- and long-term effects: the delay in an environmental impact does not lessen its magnitude. The effects of the natural selection of modified organisms also needs to be considered. Experience from the introduction of non-indigenous organisms could also usefully be built upon. The Council of Europe has already initiated work in this area.

146. Safety conditions for contained use: Much effort has been concentrated hitherto on large-scale, low-risk GMOs in containment and it is important that this work be continued. There has also been successful development of scale up techniques for low risk organisms, which demonstrates a successful approach to risk management practices. However, recognizing that certain applications necessarily depend on the use of higher risk organisms, attention could be given to, and international guidance developed for, the safe use of large-scale, higher risk organisms.

147. Standards could be developed for worker safety practices which are appropriate to certain risk categories.

148. There is also a need for international harmonization on the disposal of large quantities of GMOs. It is important that the measures ensure that GMOs from large-scale (and also small-scale) contained uses do not become accidental releases by this route and cause damage to the environment. Internationally agreed procedures for disposal and waste treatment should not only address the disposal of micro-organisms but also of other genetically modified organisms.

149. Safety conditions for release into the environment: Further work in this area is imperative, and should focus on transforming the principles into practical conditions, embracing both human health and environmental aspects: Generic practices on safety conditions for releases have to be developed and internationally harmonized.

150. The above-mentioned principles have been developed for small-scale field research. In order to maintain the step by step development, principles and protocols for safety conditions for large-scale releases could be developed. Safety conditions for both small and large-scale releases could include waste treatments, contingency plans and labelling.

151. Environmental Monitoring: Monitoring as a part of the step by step procedure (tracking the GMO and the gene) has received a fair amount of attention throughout the available documents, but further detailed exploration and harmonization of the different techniques and procedures is an important area for further work. In particular, work is needed on the detection of micro-organisms and other organisms not readily visible to the naked eye, such as fish.

152. Monitoring for possible long-term ecological impacts is still a largely under researched area which requires international attention, including fundamental research on ecosystem interactions. Work is needed to identify suitable indicator organisms for different environments. As discussed earlier, attention should be given to both short- and long-term effects. The results of monitoring need to be made widely available

153. Inspections: Main elements for further work include the establishment and development of a harmonized international approach to inspections; training on a national basis of inspectors and employee representatives to enable their involvement in inspections; and mutual recognition of inspections.

154. Contingency planning and mitigation procedures: Main elements for further work include; development of harmonized approaches to contingency planning and mitigation procedures and an international system for the exchange of information in this area, including the establishment of specialized centres.

155. Transboundary aspects. Transport: In December 1990, the United Nations Committee on the Transport of dangerous Goods recommended in principle that all GMOs be considered as pathogens for the purposes of packaging and labelling. Further international consideration needs to be given to the appropriate transportation requirements for organisms that potentially could cause adverse effects on human health or the environment.

156. There are clearly transboundary implications in the use of this technology. The ability of organisms to move, the fact that once released, they can often not be recalled, and any escape from contained use could lead to the transportation of organisms across boundaries, such as along water courses. For this reason, any information exchange network should include provision for the notification of transboundary movements and effects to potentially affected countries.

157. Role of the public: The public has a clear role to play in the wide development of biotechnology which can only develop successfully if it is overtly beneficial and safe. A central issue is necessarily that of informing the public, both about the technology itself and about particular proposed operations. The two EC directives on GMOs state which information cannot be held as confidential, and allow for the consultation of certain groups of the public during the processing of a notification concerning a GMO activity. The EC directive on access to environmental information provides a similar model: all information, other than that which is commercially confidential or relates to national security, must be made available. The OECD also has adopted a Council Recommendation on the provision of information on installations in which hazardous materials are used; the Recommendation also sets out proposals for industry and Governments with regard to the provision of information.

158. Mechanisms such as those outlined above ensure transparency. This can further be promoted by providing a role for the public in the decision-making process. For example, a key role is provided if the public have the possibility to express their views about certain proposals before final decisions are made. Involvement in this way fosters good relationships between regulatory authorities, industry and the public, and should be encouraged.
